



17 β -hydroxysteroid dehydrogenase type 10 deficiency

17 β -hydroxysteroid dehydrogenase type 10 (HSD10) deficiency is a disorder that affects many parts of the body. This condition is typically more severe in males than in females. Males with HSD10 deficiency have normal early development but soon begin to lose skills they have acquired. This developmental regression typically occurs before age 5 and results in intellectual disability and loss of motor skills such as sitting, standing, and walking. Affected males frequently have weak muscle tone (hypotonia), recurrent seizures (epilepsy), and movement problems. Progressive vision and hearing loss is also common in males with HSD10 deficiency.

Females with HSD10 deficiency may have developmental delay, learning problems, or intellectual disability, but they do not experience developmental regression. Some females may have additional features of this condition, such as epilepsy, movement problems, and hearing loss.

Frequency

The prevalence of HSD10 deficiency is unknown. At least 11 affected individuals have been identified.

Genetic Changes

Mutations in the *HSD17B10* gene cause HSD10 deficiency. This gene provides instructions for making an enzyme called HSD10, which is found in many areas of the body. The HSD10 enzyme is located within mitochondria, the energy-producing centers inside cells, where it has several different functions. This enzyme is involved in breaking down the protein building block (amino acid) isoleucine and a group of fats called branched-chain fatty acids. It is also necessary for certain chemical reactions involving male sex hormones (androgens), female sex hormones (estrogens), and substances called neurosteroids that regulate the activity of the nervous system.

Mutations that cause HSD10 deficiency change single amino acids in HSD10, which reduces or eliminates the activity of the enzyme. It remains unclear how a shortage (deficiency) of HSD10 enzyme leads to the signs and symptoms of this disorder. Some researchers suspect that the neurological problems associated with HSD10 deficiency are caused by abnormal neurosteroid activity. Other features of the disorder may be related to the inability to process isoleucine and certain fats.

Inheritance Pattern

This condition is inherited in an X-linked dominant pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is usually sufficient to cause the disorder. However, some females with one mutation do not develop any signs or symptoms of the condition. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- 2-methyl-3-hydroxybutyric aciduria
- 2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency
- 2M3HBA
- 3-hydroxy-2-methylbutyryl-CoA dehydrogenase deficiency
- 3H2MBD deficiency
- HSD10 deficiency
- hydroxyacyl-CoA dehydrogenase II deficiency
- MHBD deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C5-OH Acylcarnitine
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C5-OH.pdf>

Genetic Testing

- Genetic Testing Registry: 2-methyl-3-hydroxybutyric aciduria
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1845517/>

Other Diagnosis and Management Resources

- Baby's First Test
<http://www.babysfirsttest.org/newborn-screening/conditions/2-methyl-3-hydroxybutyric-acidemia>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Amino Acid Metabolism Disorders
<https://medlineplus.gov/aminoacidmetabolismdisorders.html>
- Health Topic: Genetic Brain Disorders
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Lipid Metabolism Disorders
<https://medlineplus.gov/lipidmetabolismdisorders.html>
- Health Topic: Newborn Screening
<https://medlineplus.gov/newbornscreening.html>

Genetic and Rare Diseases Information Center

- 2-methyl-3-hydroxybutyric aciduria
<https://rarediseases.info.nih.gov/diseases/10716/2-methyl-3-hydroxybutyric-aciduria>

Educational Resources

- MalaCards: 2-methyl-3-hydroxybutyric aciduria
http://www.malacards.org/card/2_methyl_3_hydroxybutyric_aciduria
- Medical Home Portal
<https://www.medicalhomeportal.org/newborn/2m3hba-deficiency>
- Orphanet: Short chain 3-hydroxyacyl-CoA dehydrogenase deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=35123

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)
<http://www.climb.org.uk/>
- Organic Acidemia Association
<http://www.oaanews.org>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%282-methyl-3-hydroxybutyric+aciduria%5BTIAB%5D%29+OR+%282-methyl-3-hydroxybutyryl-coa+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%282m3hba%5BTIAB%5D%29+OR+%283-hydroxy-2-methylbutyryl-coa+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%28mhbd+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- 17-BETA-HYDROXYSTEROID DEHYDROGENASE X DEFICIENCY
<http://omim.org/entry/300438>

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